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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,168	04/26/2002	Duarte Miguel Franca Teixeira Dos Praeres	Q68133	4986
23373	7590	05/11/2004	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			WEBER, JON P	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,168

Applicant(s)FRANCA TEIXEIRA DOS
PRAZERES ET AL.**Examiner**

Jon P Weber, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

Status of the Claims

Claims 1-7 have been presented for examination.

Specification

The disclosure is objected to because of the following informalities:

At page 3, "alcane" is a misspelling.

Appropriate correction is required.

Claim Objections

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Parent claim 1 is an enzymatic method, whereas dependent claim 5 is not, an impossible situation.

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Parent claim 3 is drawn to using a hydro-cyclone. It is impossible to both use the hydro-cyclone and not use it in claim 6. It is suggested that claim 6 depend from claim 1 and be edited for content.

Claims 2-7 are objected to for reciting "characterized by the fact that" which is idiosyncratic and unclear. It is suggested to substitute "wherein" for this phrase.

Claim 1 recites "crystallisation" which is a misspelling.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 provides for the use of proteases in organic media, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 6 recites "another unit" which is vague and indefinite because the metes and bounds of the claim are not clear. The disclosure provides no other methods that might be used for the separation "instead of the hydro-cyclone".

Claim 7 recites the limitation "further purified ..." in line 2. There is insufficient antecedent basis for this limitation in the claim. The claimed process is one of simultaneous synthesis and crystallization; further steps of purification would not be part of that process.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain combinations of amino acids and resulting dipeptide and conditions, does not reasonably provide enablement for any X, Y or XY or conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

As pointed out in the disclosure, it is important that the resulting dipeptide is sufficiently insoluble in the reaction solvent that it not only precipitates, but crystallizes. Accordingly, the disclosure suggests certain hydrophobic AcXOEt and certain hydrophilic YNH₂ should be mixed to form a product AcXYNH₂ that will crystallize simultaneously with formation (a list of possible products are provided on page 4). There is also considerable influence from the type and concentration ingredients, including: surfactant, alkane, alcohol, buffer, water, and enzyme.

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These must be controlled to minimize side reactions, hydrolysis of the ester and transesterification with the alcohol (page 3). The disclosure raises these issues and then fails to provide guidance other than the specific examples of how one selects the various parameters. Thus a person of ordinary skill in the art would have to experiment with these parameters to find suitable conditions, experimentation that would involve considerable inventive contribution absent guidance from the disclosure. It is this level of experimentation that is beyond routine and constitutes an undue burden.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Serralheiro et al. (1999) in view of Feliciano (2000).

Claims 1, 4 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Feliciano et al. (1997) in view of Feliciano (2000).

Serralheiro et al. (1999) disclose the simultaneous synthesis and “precipitation” of AcPheLeuNH₂ (reaction 1) from AcPheOEt and LeuNH₂ by α -chymotrypsin in reversed micelles (the product dipeptide has limited solubility in the solvent) in a Carbosep[®] ultrafiltration ceramic membrane reactor. The process was run in both batch and continuous modes (page 508). The peptide retained on the membrane was recovered by centrifugation and purified by re-

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crystallization (page 509). Feliciano et al. (2000) indicate that the solid dipeptide product that precipitates in this reaction has crystalline properties (page 265, column 1, first full paragraph).

Claims 1, 4 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Feliciano et al. (1997) in view of Feliciano (2000).

Feliciano et al. (1997) examined the α -chymotrypsin catalyzed formation of a number of dipeptides in reversed micelles. They report that about five of these dipeptides "precipitated" during synthesis from the reaction medium and were collected by centrifugation (page 289). Feliciano et al. (2000) indicate that the solid dipeptide products that precipitate in this reaction have crystalline properties (page 265, column 1, first full paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serralheiro et al. (1999), Feliciano et al. (1997) and Nagano et al. (US 5,547,858).

The teachings of Serralheiro et al. (1999) and Feliciano et al. (1997) are discussed above. Even if Serralheiro et al. (1999) and Feliciano et al. (1997) may lack a hydro-cyclone method of collecting dipeptide crystals simultaneously with their formation.

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Nagano et al. (US 5,547,858) teach using a hydro-cyclone method of collecting crystals formed simultaneously in a biological synthesis.

A person of ordinary skill in the art at the time the invention was made would have been motivated to use the hydro-cyclone method of Nagano et al. (US 5,547,858) in the process of Serralheiro et al. (1999) or Feliciano et al. (1997) to collect crystallizing dipeptide product because both of these biochemical processes produce a crystalline product whose removal is known by simple thermodynamic principles to drive the formation of further product and increase yield.

Hence it is *prima facie* obvious to use the hydro-cyclone method to collect crystals that are simultaneously formed in a biochemical reaction.

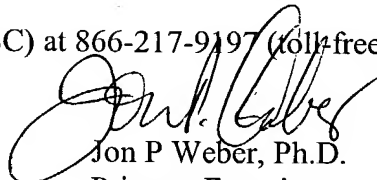
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 571-272-0925. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
5 May 2004